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Endovascular Therapy for Chronic Mesenteric Ischemia

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OBJECTIVES We sought to describe the outcomes of a consecutive series of patients with chronic mesenteric ischemia (CMI) who were treated with percutaneous stent revascularization.

BACKGROUND Historically, the treatment for CMI has been surgical revascularization. However, surgery carries a significant procedural complication rate and mortality.

METHODS Fifty-nine consecutive patients with CMI underwent stent placement in 79 stenotic (>70%) mesenteric arteries. All patients had clinical follow-up and 90% had anatomical follow-up with angiography (computed tomography or conventional) or ultrasound at ≥6 months after the procedure.

RESULTS Procedural success was obtained in 96% (76 of 79 arteries) and symptom relief occurred in 88% (50 patients). At a mean follow-up of 38 ± 15 months (range, 6 to 112 months), 79% of the patients remained alive, and 17% (n = 10) experienced a recurrence of symptoms. Angiography or ultrasound obtained at 14 ± 5 months after the procedure demonstrated a restenosis rate of 29% (n = 20). All patients with recurrent symptoms had angiographic in-stent restenosis and were successfully revascularized percutaneously.

CONCLUSIONS Percutaneous stent placement for the treatment of CMI can be performed with a high procedural success and a low complication rate. The long-term freedom from symptoms and vascular patency are comparable with surgical results. The inherent lower procedural morbidity and mortality makes the endovascular approach the preferred revascularization technique for these patients. (J Am Coll Cardiol 2006;47:944–50) © 2006 by the American College of Cardiology Foundation

Mesenteric arterial stenosis is a common finding in elderly patients with arteriosclerotic disease. Using duplex ultrasound, Hansen et al. (1) found that the prevalence of significant (>70% diameter stenosis) mesenteric artery stenosis in subjects older than 65 years of age was 17.5%. Chronic symptoms related to mesenteric arterial obstructive disease, termed chronic mesenteric ischemia (CMI), are an unusual clinical problem manifested by recurrent, debilitating abdominal pain, usually occurring after meals. In general, patients with CMI commonly have stenoses or occlusions of at least two or more mesenteric arteries, and this condition may lead to emaciation and death if left untreated (2,3). Historically, the treatment of this condition has been surgical revascularization, with a perioperative complication rate ranging between 33% and 47% and a 30-day mortality rate of 8% to 12% (4,5).

Atherosclerotic mesenteric stenoses usually are focal and most often are located at the ostium or the very proximal portion of these vessels, which makes them technically suitable for percutaneous transluminal intervention. Small case series have shown that, in selected patients, endovascular therapy is a safe and effective treatment for this condition (6,7).

Aorto-ostial stenoses, in general, are difficult to treat with balloon angioplasty alone because of the elastic recoil of the bulky plaque after balloon dilation. In renal artery atherosclerotic aorto-ostial stenoses, the use of stents has been shown to be superior to balloon angioplasty alone (8,9). It is reasonable to infer that the same may be true for the treatment of mesenteric artery stenoses; however, there are limited data in the literature addressing the role of percutaneous stent revascularization for the treatment of CMI (10,11). Therefore, the purpose of this report is to describe the outcomes of a consecutive series of patients with CMI treated with percutaneous stent revascularization.

METHODS

Patient population. From April 1993 until December of 2004, 59 consecutive patients with symptomatic mesenteric stenosis were treated endovascularly with primary stent revascularization. The indications for the procedure and the clinical presentations were categorized as: 1) typical symptoms, manifested as postprandial abdominal pain, weight loss, and/or "food fear" (12); 2) ischemic gastropathy, manifested as nausea, vomiting, fullness, abdominal pain, or weight loss (13); or 3) ischemic colitis, manifested as abdominal pain, gastrointestinal bleeding, and/or hematochezia (14). This retrospective review was approved by the investigational review board of the Ochsner Clinic Foundation.

Procedure. Fifty-nine patients with 79 stenotic mesenteric arteries were treated in 61 stent-revascularization procedures. Stenosis of the target mesenteric artery was confirmed with nonselective or selective contrast arteriography. The technique of mesenteric stent placement is similar to renal artery stent placement (15).

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Abbreviations and Acronyms

CMI = chronic mesenteric ischemia
CTA = angiographic computed tomography
SMA = superior mesenteric artery
TVR = target vessel revascularization

Retrograde common femoral arterial access was used in 77% (n = 47), and brachial artery access was employed in 23% (n = 14) of the procedures. Aspirin was begun at least one day before the procedure, with the use of clopidogrel left at the operator's discretion. Unfractionated heparin was administered to maintain an activated clotting time of ≥250 s.

Outcomes. All patients were followed for at least six months. They were asked to return to the clinic at one-month and six-month intervals after the procedure. A noninvasive imaging study (angiographic computed tomography or a duplex ultrasound) to assess the patency of the stent(s) was performed between six months and one year after the procedure, or sooner if symptoms returned. Quantitative measurement of the percent diameter stenosis of the target lesion was obtained from the invasive and noninvasive (i.e., computed tomography) angiograms (16), and estimated from duplex ultrasound velocities (17).

Definitions. Primary stent placement was defined as the intention to deploy a stent in a target mesenteric vessel before the procedure, regardless of the angiographic result after balloon predilation. Angiographic success was defined as a final diameter stenosis of <30%, and procedural success was defined as an angiographic success without an in-hospital major complication. Major complications included death, myocardial infarction, stroke, need for emergent surgical revascularization or in-hospital repeat target vessel revascularization (TVR), atheroembolization, need for blood transfusion, need for dialysis, or any vascular access complication that prolonged the hospital stay. Chronic renal insufficiency was defined as a creatinine >1.5 mg/dl. Recurrence of (ischemic) symptoms was defined as the reappearance of symptoms with similar pattern and characteristics to those that occurred before stent placement. Restenosis was defined as: 1) a >50% diameter stenosis in the follow-up angiography using computerized quantitative angiography (Image Comm Systems Inc., Mountain View, California); 2) >50% diameter stenosis by quantitative angiographic computed tomography (CTA) (16); or 3) >70% diameter stenosis by duplex ultrasound (17). Event-free survival was defined as freedom from death, recurrent ischemic symptoms, and TVR. Symptom relief was defined as resolution of the presenting symptoms causing CMI, and improvement of symptoms was defined as the persistence of symptoms causing CMI although less intense, less frequent, with a different pattern, or as the persistence of some but not all of the original symptoms.

Table 1. Clinical Characteristics

	n = 59
Age, yrs	67 ± 11
Gender, female (%)	38 (64)
Hypertension (%)	49 (83)
Diabetes mellitus (%)	14 (24)
Hypercholesterolemia (%)	55 (93)
Current tobacco abuse (%)	25 (42)
Coronary artery disease (%)	48 (81)
Peripheral vascular disease (%)	40 (68)
CRI (%)	16 (27)
Renal artery stenosis (%)*	32 (54)
Neurovascular disease (%)	20 (34)
% EF	45 ± 13 (range: 10 to 60)
% EF <40 (%)	27 (46)
Previous MI (%)	24 (41)
Previous stroke (%)	7 (12)

*>50% diameter stenosis.
CRI = chronic renal insufficiency; EF = ejection fraction; MI = myocardial infarction.

Statistical analysis. Categorical variables are reported as frequencies and percentages and continuous variables as mean ± standard deviation. Student *t* tests were used to compare continuous variables and chi-square tests were used to compare categorical variables. Probability of survival and symptom-free survival were calculated using Kaplan-Meier survival curves (version 11.0, SPSS Inc., Chicago, Illinois). Differences at the level of $p < 0.05$ (two-tailed) were considered as statistically significant.

RESULTS

The baseline clinical characteristics of the patient population are shown in Table 1.

Clinical presentation and angiographic characteristics. Forty-six patients (78%) presented with typical symptoms of CMI (Fig. 1, Table 2), eight patients (14%) presented with symptoms suggestive of ischemic gastropathy or celiac territory ischemic syndrome (Fig. 2), and five patients (8%) presented with ischemic colitis (confirmed colonoscopy and biopsy) (Fig. 3). The angiographic characteristics and results are shown in Table 3. The celiac artery was treated in 47% (n = 37), the superior mesenteric artery (SMA) in 40.5% (n = 32), and the inferior mesenteric artery in 10% (n = 8) of the cases. In addition, one vein graft and one common hepatic artery arising from the aorta were also treated. Single vessel stenting was performed in 71% (n = 41) and multivessel stent placement in 29% (n = 17) of the patients.

In-hospital outcomes. A total of 88 stents (85 balloon-expandable and 3 self-expandable stents) were successfully implanted in 77 mesenteric arteries. Angiographic success was obtained in 97% (77 of 79 vessels), and procedural success in 96% (76 of 79 vessels). One failure occurred in a patient with chronic complete occlusion of all mesenteric vessels; attempts to cross the occlusions with a guidewire failed, and the patient was referred for surgical revascularization. The second failure was an in-hospital death of

Figure 1. A 72-year-old male patient with typical symptoms of chronic mesenteric ischemia.

a malnourished diabetic patient with chronic renal insufficiency who, after stenting, developed renal and multiorgan failure. Procedural complications included two brachial arterial-access thromboses successfully treated percutaneously.

Symptom relief occurred in 88% (n = 50) of the patients with a successful procedure (n = 57). In seven patients, there was partial or no symptom relief: three (5%) patients from the group with typical symptoms and four patients (7%) from the ischemic gastropathy group.

There were four patients with angiographic evidence of extrinsic compression of the celiac artery by the arcuate ligament of the diaphragm (typical angiographic features), and one of these patients also had a severe stenosis of the SMA. One of these four patients presented with ischemic colitis (Fig. 4), and the other three patients presented with postprandial abdominal pain (one had erosive gastritis). In all four of these patients, the procedures were successful and the symptoms were relieved after revascularization.

Table 2. Initial Clinical Presentation

	n = 59
Abdominal pain (%)	59 (100)
Postprandial abdominal pain (%)	46 (78)
Weight loss (%)	40 (68) (23 ± 12 lbs)
Nausea/vomiting/fullness (%)	13 (22)
Diarrhea/constipation (%)	13 (22)
Hematochezia/lower gastrointestinal bleeding (%)	5 (8)

Follow-up. At a mean follow-up of 38 ± 15 months (range, 6 to 112 months), of the 57 patients with a successful procedure who left the hospital, 46 (81%) remained alive. The 11 deaths were not related to recurrent mesenteric ischemia (Table 4), and seven patients had anatomical follow-up prior to their death.

Of the 57 patients (76 arteries) with a successful procedure discharged from the hospital, anatomical follow-up was available in 52 patients (91%) and 69 vessels (90%) at 14 ± 5 months after the procedure (range, 6 to 26 months). Angiography was obtained in 18 patients, CTA in 27 patients, and duplex ultrasound in 7 patients. In-stent restenosis occurred in 20 of the 69 arteries (29%). There were no cases of in-stent occlusion, and only 10 patients with recurrence of symptoms required repeat percutaneous revascularization.

The primary patency rate at 14 ± 5 months was 71%, and the primary assisted patency rate was 83%. There was no difference in the restenosis rate between the celiac artery (29%) and the SMA (30%; p = 0.51). Recurrence of ischemic symptoms occurred in 10 (17%) patients at 6.8 ± 4 months after the procedure (range, 2 to 14 months). Nine of these 10 patients (90%) had a single-vessel stent placement. Symptom recurrence tended to be more frequent

Figure 2. A 61-year-old woman with symptoms of ischemic gastropathy for more than one year and occlusion of all three mesenteric arteries. The superior mesenteric artery was successfully recanalized and stented, with immediate resolution of her symptoms.

among patients who underwent single-vessel revascularization (24%), than in patients receiving more than one-vessel revascularization (6%; $p = 0.09$). In-stent restenosis was confirmed with angiography in every patient with symptom recurrence. In eight (80%) patients, recurrence of symptoms occurred in the first nine months after stent placement. The five-year probability of survival (72%), freedom from recurrence of symptoms (80%) and symptom-free survival (57%) using Kaplan-Meier survival analysis are shown in Figure 5.

The 10 patients with symptom recurrence (10 vessels) underwent TVR with balloon angioplasty alone (n = 4), balloon angioplasty and brachytherapy (n = 3), or re-

Figure 3. A 67-year-old man with ischemic cardiomyopathy who developed abdominal pain and lower gastrointestinal bleeding. Mesenteric angiography showed high grade stenosis of the celiac trunk and inferior mesenteric arteries, which were successfully stented with resolution of symptoms. A two-year follow-up angiogram revealed patent mesenteric stents **(last upper and lower panels on the right)**.

Table 3. Quantitative Angiography in 59 Patients and 79 Mesenteric Arteries

Three-vessel disease (%)	25 (42)
Two-vessel disease (%)	31 (53)
One-vessel disease (%)	3 (5)
Ostial stenosis (%)	64 (81)
Nonostial stenosis (%)	15 (19)
Chronic total occlusion (%)	4 (5)
RVD baseline, mm	6.20 ± 1.1
MLD baseline, mm	1.26 ± 0.4
% DS baseline	80 ± 6
RVD postintervention, mm	6.21 ± 1.1
MLD postintervention, mm	5.82 ± 1.0
% DS postintervention	7 ± 15

DS = diameter stenosis; MLD = minimal lumen diameter; RVD = reference vessel diameter.

Table 4. Overall Survival and Clinical Events of 58 Patients With Initial Angiographic Success

	n = 58
Death (%)	12 (21)
MI	6
Cancer*	4*
Renal failure/sepsis	1
Stroke	1
Mesenteric ischemia	0
Recurrence of symptoms (%)	10 (17)
Death or recurrence of symptoms (%)	21 (36)
Event-free survival (%)	37 (64)
Restenosis (%) by patient†	19 (37)*
Restenosis (%) by vessel†	20 (29)*

*One patient developed symptomatic in-stent restenosis 11 months before death; treated successfully percutaneously. †A total of 52 patients and 69 vessels with anatomical follow-up at 14 ± 5 months after the procedure.

stenting (n = 3) with relief of symptoms. Of these 10 patients, 3 patients developed a second restenosis with recurrence of symptoms and were successfully treated with balloon angioplasty; the other 7 patients have remained asymptomatic.

DISCUSSION

The use of percutaneous revascularization in the mesenteric circulation has been reported in small series with relatively short follow-up. These studies have shown that balloon angioplasty yields a high procedural success, with low morbidity and mortality rates, suggesting that endovascular therapy is an important alternative treatment to surgical revascularization in selected patients (6,7). There are limited data describing endovascular stents for the treatment of mesenteric stenosis (10,11). In a recent study (11) of 25 patients and 26 arteries treated with primary stenting, technical success was obtained in 96% and relief of symptoms in 88%. There was no procedural mortality, and the only complications were the development of a pseudoaneurysm (n = 2), and renal failure (n = 1).

The present study constitutes the largest series of patients with CMI treated with a strategy of primary stent placement. The patient population had significant comorbidities, including coronary and peripheral vascular disease, as well as ischemic cardiomyopathy and, similar to previous reports, more than half of the patients had concomitant renal artery stenosis (18). The diagnosis of CMI had been made by a gastroenterologist, primary care physician, and/or vascular surgeon before the procedure, and in every case there was consensus to proceed with intervention. It is important to stress the need for a multidisciplinary approach in the treatment of this challenging condition (19). In this series, 22% of the patients did not have the classic presentation of intestinal angina and weight loss.

Clinical presentation and in-hospital outcomes. The classic triad of postprandial abdominal pain, weight loss, and fear for occurs in 50% to 70% of the patients (2). More recently, ischemic gastropathy (13,20,21), which is manifested by nausea, vomiting, fullness, epigastric pain, weight loss, and gastric ulcers, and ischemic colitis (14,22), which presents as lower abdominal pain and diarrhea followed by gastrointestinal bleeding or hematochezia, have been shown to be manifestations of CMI. In the present series, 14% of the patients presented with ischemic gastropathy and 8% with ischemic colitis.

Figure 4. A 38-year-old woman with extrinsic compression of the celiac trunk and history of crampy abdominal pain and bloody diarrhea. The patient refused surgical decompression and underwent successful stent placement with resolution of symptoms. The six-month angiographic computed tomography scan **(last panel on the right)** revealed >50% in-stent restenosis but patency of the stent and no inspiratory collapse. She has had no recurrence of symptoms at follow-up more than three years later.

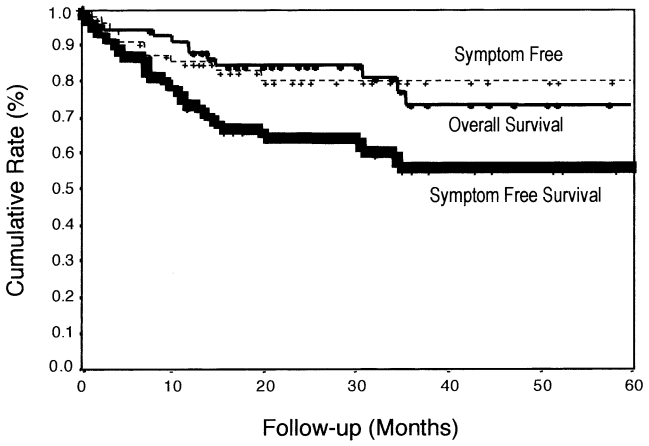

Figure 5. Kaplan-Meier survival curves showing the five-year cumulative probability of survival, symptom-free, and symptom-free survival of the 59 patients.

Symptom relief was obtained in 88%. Despite clinical consensus regarding the diagnosis and decision to proceed with intervention, it is likely that, in 12% of the patients, CMI was not the etiology or at least the only cause for the patients' symptoms.

Follow-up, late survival, and in-stent restenosis. The five-year cumulative freedom from death, symptom-recurrence, or both were 72%, 79%, and 57%, respectively (Fig. 5). These late results are comparable or in some cases superior to published surgical studies, which have reported mortality rates of 31% to 48% and symptoms recurrence of 19% to 26.5% at a follow-up of three to five years (4,5,23,24).

A restenosis rate of 29% in the present study was unexpected because, in renal arteries, which are anatomically very closely located, the reported restenosis rate after stent placement is in the low teens (9). This restenosis rate, however, is comparable with that found after surgical endarterectomy in which restenosis was found in 22% of 18 asymptomatic patients tested with duplex ultrasound (5). Whether drug-eluting stents may have a favorable impact in restenosis in the mesenteric arterial circulation remains speculative.

Despite this angiographic restenosis rate, only 17% of patients developed recurrent symptoms and required TVR. It is likely that complete revascularization may have played an important role in preventing symptom-recurrence because there was a trend toward less recurrence of symptoms in patients with multivessel stenting (6%) compared with single- vessel stenting (25%; $p = 0.09$).

In no single case did the development of in-stent restenosis lead to mortality. Surgical studies have shown that graft failure often presents abruptly as sudden occlusion, either in the early postoperative period or at follow-up, leading to bowel infarction and death in the majority of the patients (4,5,24). In contrast, none of our patients developed acute mesenteric ischemia, either early after the procedure or at follow-up. There were no acute or subacute post-procedural stent thrombosis events, and the cases of in-stent restenosis led to gradual development of symptoms.

Study limitations. This is a single center retrospective study and carries the inherent limitations of retrospective data analysis. In addition we did not directly compare endovascular treatment to surgical revascularization.

Conclusions. In the largest series of CMI patients treated with endovascular therapy studied to date, we have shown that stent placement is a safe and effective revascularization treatment. The long-term benefits and symptom-recurrence were comparable with those reported with surgical revascularization but, in contrast to surgery, in no single case did in-stent restenosis lead to acute mesenteric ischemia or death. On the basis of these results, we conclude that stent revascularization should be considered as an alternative to surgery in patients with CMI and the treatment of choice for patients who are at increased risk for surgical complications.

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